Citation:

George SM, Mayne ST, Leitzmann MF, Park Y, Schatzkin A, Flood A, Hollenbeck A, Subar AF. Dietary glycemic index, glycemic load, and risk of cancer: a prospective cohort study*Am J Epidemiol.* 2009 Feb 15;169(4):462-72.

PubMed ID: 19095757

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The primary objective of this analysis was to investigate whether glycemic index and glycemic load are related to increased risk of developing a primary cancer in a prospective cohort of women and men aged 50 years or older.

Inclusion Criteria:

Participants of the National Institutes of Health (NIH)-AARP Diet and Health Study inititated in 1995-1996.

Exclusion Criteria:

Among the 566,402 participants, those excluded from this study included those who:

- indicated that they were proxies for the intended respondents (n = 15,760)
- had any prevalent registry-reported cancer except nonmelanoma skin cancer at baseline (n = 1,875)
- self-reported cancer on the baseline questionnaire (n = 49,318)
- self-reported end-stage renal disease at baseline (n = 997)
- cancer cause-of-death record and no cancer registry record (n = 3,876)
- reported extreme intakes of total energy (n = 4,382)
- self-reported diabetes at baseline (n = 44,017)

For separate analysis of cancers of the ovary and uterus, also excluded were women who had undergone bilateral oophorectomy (n = 52,499) or hysterectomy (n = 95, 857) at baseline

Description of Study Protocol:

Recruitment

Participants from the National Institutes of Health (NIH) - AARP Diet and Health Study initiated in 1995-1996 with the mailing of a self-administered questionnaire to 3.5 million AARP members aged 50-71 years from six US states (California, Florida, Louisiana, New Jersey, North Carolina and Pennsylvania) and two metropolitan areas (Atlanta, Georgia and Detroit, Michigan).

Design: Prospective Cohort Study

The authors analyzed associations among glycemic index, glycemic load, and risk of cancer in women and men in the National Institutes of Health (NIH) - AARP Diet and Health Study.

Blinding Used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

Multivariate relative risks and 2-sided 95% confidence intervals were estimated with Cox proportional hazards models by using the SAD PROC PHREG procedure.

Data Collection Summary:

Timing of Measurements

Dietary intake assessed at baseline. Participants were followed from 1995 to 2003.

Dependent Variables

- Cancer ascertainment: cases were identified through probabilistic linkage with 11 state cancer registry databases.

Independent Variables

- Dietary assessment: dietary intakes were assessed with a self-administered 124-item food frequency questionnaire.
- Values for glycemic index and glycemic load were derived from the US Department of Agriculture (USDA) 1194-1996 Continuing Survey of Food Intakes by Individuals (CSFII) which was condensed into 225 nutritionally similar food groups.
- Using the published glycemic values compiled by Foster-Powell et al, glycemic index values were linked to each individual CSFII foods in these food groups.

Control Variables

- The baseline questionnaire also queried demographic characteristics, medical history and lifestyle.
- All models were adjusted for age, race/ethnicity, education, marital status, BMI, family history of any cancer, total energy intake, physical activity, smoking, alcohol consumption, and menopausal hormone therapy use among women

Description of Actual Data Sample:

Initial N: 262,642 men and 183,535 women

Attrition (final N): as above

Age: see below

Ethnicity: see below

Other relevant demographics:

Characteristics of Study Participants (Men: n = 262,642; Women: n = 183,535) by Quintiles of Glycemic Load and Glycemic Index

	Glycemic Load Men Quintile 1	Glycemic Load Men Quintile 5	Glycemic Load Women Quintile 1	Glycemic Load Women Quintile 5	Energy Adjusted Glycemic Load Men Quintile 1	Energy Adjusted Glycemic Load Men Quintile 5	Energy Adjusted Glycemic Load Women Quintile 1	Energy Adjusted Glycemic Load Women Quintile 5	Glycemic Index Men Quintile 1	Glycemic Index Men Quintile 5	Glycemic Index Women Quintile 1	Glycemic Index Women Quintile 5
Median glycemic load	68.0	197.2	54.1	163.9					106.4	132.6	87	106.3
Median, glycemic index	53.4	55.1	52.7	54.4					49.6	58.5	48.8	58.2
Age, years	62.3	61.4	62.0	61.3	61.8	61.8	61.5	61.6	62.1	61.7	61.9	61.4
White, non-Hispanic, %	92.3	91.0	90.7	84.6	95.3	89.4	92.8	94.3	92.9	90.9	90.5	87.5
College or postcollege, %	69.9	59.6	56.2	49.4	70.3	61.7	57.6	50.8	72.2	56.0	63.2	43.6
Married, %	82.1	85.0	40.8	44.0	82.0	85.8	46.0	42.3	81.3	86.3	41.4	44.9
Body Mass Index <25, %	26.8	30.4	45.5	40.9	24.8	36.3	43.4	47.3	31.2	30.9	50.2	41.1
Family history of any cancer, %	45.8	46.9	51.0	50.2	47.5	46.5	51.3	50.5	46.4	47.1	50.5	51.1
Current smoker, %	10.0	13.1	16.9	14.9	16.9	9.2	22.3	12.1	7.8	17.0	10.4	21.9
Physical Activity ≥5 times/week, %	16.9	25.8	13.9	18.6	18.6	26.3	14.7	18.8	26.0	16.7	23.6	11.0
Alcohol ≥15 g/day, %	29.7	26.0	14.2	8.2	65.5	11.9	33.4	2.6	38.2	18.4	12.6	8.6
Carbohydrates, total g/day	134.2	419.5	106.7	355.0	224.2	364.1	198.6	291.3	258.2	270.8	213.2	221.5
Dietary fiber, g/day	11.6	30.7	9.8	27.3	19.3	25.6	17.7	21.3	25.5	16.2	22.1	13.8
Current menopausal hormone therapy, %			46.0	39.8			45.6	41.5			47.1	40.3
Total energy, kcal/day	1,189.4	3,127.2	893.8	2,475.8	2,349.3	2,386.8	1,848.9	1,804.3	2,099.4	2,099.4	1,499.9	1,651.6

Anthropometrics

Location: United States

Summary of Results:

Glycemic Index in Relation to Cancer Incidence Among US Women in the NIH-AARP Diet and Health Study, 1995-2003

Type of Cancer	No. of Events	Quintile 1(33.61-50.43) Relative Risk	Quintile 2 (50.44-52.56) Relative Risk	Quintile 2 95% CI	Quintile 3 (52.57-54.39) Relative Risk	Quintile 3 95% CI	Quintile 4 (54.4-56.55) Relative Risk	Quintile 4 95% CI	Quintile 5 (56.56-83.94) Relative Risk	Quintile 5 95% CI	Ptrend
Breast	5,478	1.00	0.97	0.89, 1.05	1.02	0.94, 1.11	1.02	0.94, 1.11	1.05	0.97, 1.15	0.129
Colorectal	1,457	1.00	0.94	0.80, 1.12	1.06	0.90, 1.25	1.08	0.91, 1.27	1.16	0.98, 1.37	0.026
Endometrial	1,041	1.00	0.97	0.80, 1.17	0.91	0.75, 1.10	0.91	0.75, 1.11	0.85	0.70, 1.04	0.094
Non-Hodgkins' lymphoma	605	1.00	0.96	0.74, 1.25	1.05	0.81, 1.36	1.03	0.78, 1.36	0.92	0.70, 1.21	0.680
Melanoma	543	1.00	0.98	0.76, 1.27	1.06	0.82, 1.36	0.99	0.76, 1.29	0.77	0.57, 1.03	0.136
Ovarian	475	1.00	1.12	0.85, 1.48	1.01	0.76, 1.34	0.99	0.74, 1.33	0.90	0.67, 1.23	0.371
Kidney	322	1.00	0.94	0.67, 1.33	0.99	0.70, 1.40	0.88	0.63, 1.26	0.84	0.59, 1.21	0.321
Thyroid	176	1.00	1.01	0.63, 1.61	1.02	0.64, 1.63	1.13	0.71, 1.79	0.92	0.56, 1.50	0.878
Brain	146	1.00	1.75	1.02, 3.00	1.46	0.84, 2.55	1.40	0.80, 2.47	1.26	0.70, 2.28	0.790
Myeloma	157	1.00	0.81	0.50, 1.33	1.03	0.65, 1.64	0.83	0.51, 1.36	0.73	0.43, 1.24	0.294
Stomach	127	1.00	1.06	0.61, 1.84	0.70	0.38, 1.31	1.27	0.74, 2.17	1.12	0.64, 1.97	0.520
Myeloid leukemia	119	1.00	1.33	0.76, 2.33	0.67	0.35, 1.31	1.04	0.58, 1.89	1.28	0.72, 2.88	0.601
Liver	72	1.00	1.91	0.95, 3.87	1.23	0.57, 2.64	0.62	0.25, 1.52	0.95	0.43, 2.10	0.209
Lung	2,288	1.00	1.07	0.93, 1.22	1.01	0.88, 1.16	0.98	0.86, 1.13	1.12	0.98, 1.27	0.210
Pancreas	348	1.00	0.90	0.64, 1.27	1.04	0.75, 1.44	0.90	0.64, 1.26	1.00	0.71, 1.40	0.970
Head and neck	300	1.00	0.88	0.61, 1.28	0.82	0.56, 1.19	0.88	0.61, 1.27	0.94	0.66, 1.34	0.834
Bladder	235	1.00	1.13	0.76, 1.68	0.82	0.53, 1.26	0.96	0.64, 1.45	0.91	0.60, 1.38	0.483
Esophagus	76	1.00	0.95	0.43, 2.08	1.10	0.51, 2.35	1.43	0.70, 2.92	1.27	0.60, 2.67	0.332
All cancers	15,215	1.00	0.99	0.94, 1.04	1.01	0.96, 1.06	0.99	0.94, 1.04	1.03	0.98, 1.09	0.217

Glycemic Index in Relation to Cancer Incidence Among US Men in the NIH-AARP Diet and Health Study, 1995-2003

Type of Cancer	No. of Events	Quintile 1 (33.51-51.26) Relative Risk	Quintile 2 (51.27-53.32) Relative Risk	Quintile 2 95% CI	Quintile 3 (53.33-55.04) Relative Risk	Quintile 3 95% CI	Quintile 4 (55.05-57.01) Relative Risk	Quintile 4 95% CI	Quintile 5 (57.02-84.13) Relative Risk	Quintile 5 95% CI	Ptrend
Prostrate	15,949	1.00	0.99	0.94, 1.04	1.02	0.98, 1.08	1.05	1.00, 1.10	0.98	0.93, 1.03	0.946
Colorectal	3,031	1.00	0.99	0.89, 1.12	1.01	0.90, 1.14	1.04	0.93, 1.17	1.16	1.04, 1.30	0.007
Advanced Prostrate	1,656	1.00	0.92	0.79, 1.07	1.00	0.86, 1.16	0.96	0.82, 1.12	0.93	0.79, 1.09	0.509
Melanoma	1,485	1.00	1.07	0.91, 1.25	1.09	0.93, 1.27	1.00	0.85, 1.18	1.07	0.90, 1.27	0.680
Non-Hodgkin's lymphoma	1,114	1.00	0.870	0.72, 1.06	0.96	0.79, 1.16	0.91	0.74, 1.10	0.79	0.65, 0.96	0.035
Kidney	857	1.00	0.99	0.79, 1.23	0.99	0.80, 1.23	1.15	0.93, 1.43	1.05	0.84, 1.31	0.368

Stomach	440	1.00	1.44	1.04, 1.99	1.29	0.93, 1.80	1.54	1.12, 2.12	1.50	1.09, 2.08	0.020
Brain	356	1.00	1.07	0.76, 1.45	0.70	0.50, 0.99	0.98	0.71, 1.34	0.70	0.49, 0.99	0.043
Myeloma	331	1.00	0.92	0.65, 1.30	1.09	0.78, 1.52	1.05	0.75, 1.47	0.85	0.59, 1.23	0.614
Myeloid leukemia	288	1.00	0.99	0.69, 1.41	0.82	0.57, 1.20	1.02	0.72, 1.45	0.70	0.47, 1.03	0.117
Liver	238	1.00	1.73	1.13, 2.63	1.24	0.79, 1.95	1.17	0.74, 1.85	1.62	1.05, 2.48	0.185
Thyroid	153	1.00	1.02	0.62, 1.66	1.19	0.74, 1.92	0.81	0.48, 1.38	0.79	0.46, 1.37	0.300
Lung	3,769	1.00	1.00	0.89, 1.11	1.04	0.93, 1.16	1.00	0.90, 1.11	1.08	0.98, 1.20	0.137
Bladder	1,246	1.00	1.13	0.94, 1.36	1.07	0.89, 1.29	1.04	0.86, 1.25	1.29	1.07, 1.54	0.023
Head and Neck	939	1.00	0.96	0.78, 1.17	0.78	0.63, 0.97	0.93	0.76, 1.14	0.91	0.74, 1.11	0.365
Pancreatic	601	1.00	0.97	0.74, 1.27	1.19	0.93, 1.54	1.05	0.81, 1.37	1.19	0.92, 1.55	0.160
Esphagus	425	1.00	1.23	0.89, 1.7	1.03	0.74, 1.44	1.24	0.90, 1.71	1.50	1.10, 2.05	0.013
All Cancers	33,203	1.00	1.01	0.98, 1.05	1.02	0.98, 1.05	1.03	1.00, 1.07	1.04	1.00, 1.08	0.012

Key Findings

From 1995 through 2003, 15,215 cancer cases in women and 33,203 cancer cases in men were identified.

For women and men, respectively, the relative risks for total cancer for high versus low glycemic index were 1.03 (P for trend = 0.217) and 1.04 (P for trend = 0.012) and, for glycemic load, were 0.90 (P for trend = 0.024) and 0.93 (P for trend = 0.01).

Associations with total cancer held only among the overweight for glycemic index and among those of healthy weight for glycemic load.

Author Conclusion:

In summary, analysis of the NIH-AARP cohort did not provide strong evidence that diets high in glycemic index and glycemic load are associated with cancer incidence. With a widening understanding of the complex interactions involved in cancer etiology and that food is not consumed in isolation, the authors believe that identification of the role of glycemic load as part of an overall healthy dietary pattern may enable examination of the broader diet-cancer relation.

Reviewer Comments:

Authors note the following limitations:

- *Narrow range of glycemic index values in the NIH-AARP cohort, which may have precluded the ability to detect the effects of different levels of glycemic index*
- *Systematic, multivariate measurement error from imprecise dietary measurements may have occurred*
- *Assessment of diet may not have captured the cancer relevant-period of exposure, given cancer's potential for long latency and the modeling based on median quintiles of dietary glycemic load at baseline*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	???
	7.5.	Was the measurement of effect at an appropriate level of precision?	???
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes